IJC Heart & Vasculature 22 (2019) 31–34

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: http://www.journals.elsevier.com/ijc-heart-and-vasculature

Prognostic impact of bundle branch block after acute coronary syndrome. Does it matter if it is left of right?

Ana Teresa Timóteo *,[1], Tiago Mendonça [1], Sílvia Aguiar Rosa [1], António Gonçalves [1], Ramiro Carvalho [1], Maria Lurdes Ferreira [1], Rui Cruz Ferreira [1]

Cardiology Department, Santa Marta Hospital, Central Lisbon University Hospital, Lisbon, Portugal

ARTICLE INFO

Article history:
Received 6 September 2018
Received in revised form 2 October 2018
Accepted 14 November 2018
Available online xxxx

Keywords:
Acute coronary syndromes
Bundle branch block
Prognosis

ABSTRACT

Background: In previous guidelines, acute coronary syndromes (ACS) with new or presumably new left bundle branch block (LBBB) were an indication for reperfusion treatment, preferably with primary angioplasty. Recent guidelines also included the presence of right bundle branch block (RBBB) in this recommendation. It was our objective to evaluate in a population of patients with ACS the differential impact of RBBB and LBBB in prognosis.
Methods: Consecutive patients included prospectively in a single-centre registry of ACS were included in the study. Patients were analyzed according to baseline ECG characteristics (normal QRS, LBBB or RBBB). Primary outcome was all-cause mortality at one-year follow-up. We used Cox-proportional hazards models to assess the predictive value for the primary outcome.
Results: A total of 3990 patients were included in, with a mean age of 64 (13) years, 72% males, 3.4% with LBBB and 4.3% with RBBB. Patients with BBB were older, with more previous history of myocardial infarction and coronary revascularization and higher prevalence of cardiovascular risk factors (except smoking). Medical treatment was similar but they were less often submitted to angioplasty. In univariate analysis, BBB patients had worst outcome (Log-rank, $p < 0.001$), but similar in LBBB and RBBB (Log-rank, $p = 0.597$). In multivariate analysis, only RBBB (HR 1.66, 95%CI 1.14–2.40, $p = 0.007$) is an independent predictor of all-cause mortality.
Conclusions: Patients with BBB have worst outcome after an ACS, particularly with RBBB. For that reason, we should pay special attention and treat these patients as aggressively as patients with normal QRS duration or LBBB.

1. Introduction

Cardiovascular diseases, particularly acute coronary syndromes (ACS), are an important cause of death in Europe [1]. Although mortality rates of ACS decreased in the last decades, due to major improvements in treatment, it stabilized in 3–5% [2]. Some special subsets of patients are at particularly risk and treatment must be optimized in those subgroups.

In previous guidelines, treatment of patients with new or presumably new left bundle branch block (LBBB) should follow recommendations for ST-segment elevation acute myocardial infarction (STEMI), with immediate reperfusion therapy, preferably primary angioplasty [3]. In recent guidelines, this recommendation has been enlarged for right bundle branch block (RBBB) patients [4,5]. However, for RBBB, evidence is less robust, with fewer available clinical studies and a lower level of evidence. The prevalence of RBBB in the context of ACS is 6–10% [6–12]. In fibrinolysis era, both BBB types had high in-hospital mortality, of around 15–20%, much higher when compared to STEMI patients or other ACS with normal QRS duration [6–8]. In more contemporaneous studies, hospital mortality is still highest in patients with BBB, particularly new-onset RBBB [9–12]. However, those studies have several limitations. Some are derived from small samples, others were performed in non-contemporaneous populations or in randomized (not real-life) populations, some are meta-analysis and, in some cases, there are important ethnical differences.

For that reason, it was our objective to assess, in a contemporaneous real-life population of patients admitted with ACS, the differential impact of LBBB and RBBB in outcome.

1.1. Population and methods

In the present study, we included consecutive adult patients admitted at the Intensive Care Unit of our Cardiology Department with an ACS, between January 2005 and November 2016. Inclusion criteria were a history of chest pain at rest or other symptoms suggestive of an ACS 48 h before admission, with or without new or presumed new significant ST-segment or T-wave changes, LBBB and/or elevated

* Corresponding author at: Serviço Cardiologia, Hospital Santa Marta, Centro Hospitalar Universitário Lisboa Central, Rua Santa Marta, 1169-024 Lisboa, Portugal.
E-mail address: ana_timoteo@yahoo.com (A.T. Timóteo).
[1] This author takes responsibility for all aspects of reliability and freedom from bias of the data presented and their discussed interpretation.

https://doi.org/10.1016/j.ijcha.2018.11.006
2352-9067/

biomarkers of myocardial necrosis (with a rise and/or fall of levels). Acute myocardial infarction was defined according to type 1 myocardial infarction universal definition [13]. STEMI was defined by the presence of persistent (>30 min) ST-segment elevation. All other cases were considered non-ST-segment elevation ACS (NSTACS).

Patients were included prospectively in the centre's ACS registry. Data was collected in a dedicated computer database. It included demographic data, clinical and patient management information, as well as in-hospital outcome. Hypertension, diabetes and hyperlipidemia were defined as previously known or on specific therapy. If the patients had smoked during the previous six months, they were classified as smokers and were self-reported. All decisions on patient management strategy (including referral for an invasive strategy and type of revascularization) were left to the attending physician.

Follow-up was obtained by a dedicated nursing team in every patient that survived to discharge and was obtained by telephone interview with the patient or with a close family member and/or by review of the medical record. Follow-up was completed in 99.7% of patients. Our primary endpoint was all-cause mortality during one-year follow-up, counted from admission. Mortality was also analyzed during hospital stay and at 30-day follow-up. Mean hospital stay was 8 days, with a median stay of 6 days and interquartil range of 5–9 days.

The authors assert that all procedures contributing to this work comply with the ethical standards of Helsinki Declaration of 1975 and that this research does not involve human and/or animal experimentation.

1.2. Statistical analysis

Patients were divided in three groups according to the presence of LBBB, RBBB or normal QRS duration in the admission ECG. Normality of continuous variables was tested with the Kolmogorov-Smirnov's test and homogeneity of variance was tested with Leven's test. All continuous variables showed normal distribution. Continuous variables are reported as mean and standard deviation (SD) and were compared with ANOVA-test. Categorical variables are reported as percentages and differences between-groups were tested with the chi-square test or Fischer's exact test, as appropriate.

Survival analysis was tested with Kaplan-Meier curves and with Log-rank test. We used Cox-proportional-hazards regression models to identify potential predictors of the primary outcome. We set a p level for inclusion in the multivariate model at 0.05. The estimates of the association between predictors and outcome are presented as hazard ratios (HR) and 95% confidence intervals (CI).

For all statistical analysis, we used the IBM SPSS statistical software package (version 19.0.0.2). All tests were two-sided with a critical value of 0.05 for statistical significance.

2. Results

We included in the present study 3990 patients. QRS duration was normal in the majority of patients. LBBB was present in 3.4% and RBBB in 4.3% of patients. Mean age was 64 (13) years, with a predominance of male gender (72%). Patients with BBB were older and had more cardiovascular risk factors, particularly LBBB patients, with the exception of smoking that was less prevalent in both BBB groups, mainly in LBBB patients (Table 1). RBBB group had more male patients, followed by normal QRS group. Regarding previous medical history, baseline characteristics were also significantly worse in both groups of BBB, particularly in LBBB group, with more frequent history of myocardial infarction and myocardial revascularization. Killip class on admission was also worse in BBB groups. Heart rate and SBP was higher in LBBB.

Pharmacological treatment was similar in all groups; however, coronary angioplasty was less performed in patients with BBB, particularly LBBB (Table 2). Thrombolysis was used in 5.3% of all patients (8.1% of STEMI cases), 3% in RBBB group, 3% in LBBB group and 5% in the group with normal QRS, with most cases being referred to our department for rescue PCI. Complications occurred at a similar rate across all groups, with the exception of cardiac arrest, more frequent in RBBB group. All mortality endpoints were more frequent in BBB, but slightly higher in the RBBB group. In univariate survival analysis, BBB patients had worse outcome (Log-rank, $p < 0.001$), but similar in LBBB and RBBB (Log-rank, $p = 0.597$).

Patients with RBBB and NSTACS, compared to patients with STEMI, have more frequently hypertension, previous revascularization, higher systolic blood pressure on admission and better Killip class (Supplemental Table). They received more often statins but were less often submitted to coronary angioplasty. Mortality was higher than usual in both groups (STEMI and NSTACS), particularly in the STEMI group.

In Cox-proportional hazards univariate analysis, both LBBB and RBBB were predictors of all-cause mortality at one-year follow-up (Table 3). The other potential predictors of outcome were age, diabetes,

Table 1
Baseline characteristics.

	Total $n = 3990$	LBBB $n = 135$	RBBB $n = 172$	Normal QRS $n = 3683$	*p*-value
Age (years)	64 (13)	72 (10)	70 (11)	63 (13)	<0.001
Male gender (%)	72.0	61.9	74.4	72.3	0.025
Risk factors (%)					
Hypertension	64.5	81.5	70.3	63.6	<0.001
Hyperlipidemia	51.3	60.7	54.7	50.8	0.052
Diabetes	25.8	43.0	34.3	24.8	<0.001
Smoking	38.4	15.6	26.2	39.8	<0.001
Previous history (%)					
Myocardial infarction	14.5	31.1	19.2	13.7	<0.001
PCI	10.7	17.8	13.4	10.3	0.012
CABG	3.7	14.8	5.8	3.2	<0.001
Stroke/TIA	5.7	9.6	6.4	5.5	0.113
PAD	3.5	3.7	4.1	3.4	0.890
COPD	2.1	4.4	1.7	2.0	0.143
STEMI (%)	65.1	–	51.7	67.0	<0.001
Heart rate (bpm)	78 (20)	89 (21)	82 (22)	78 (20)	<0.001
SBP (mmHg)	137 (29)	144 (33)	135 (32)	137 (29)	<0.019
Killip class ≥2 (%)	14.8	40.0	23.3	13.4	<0.001
Qualitative LVEF (%)					<0.001
>50%	56.2	28.1	54.7	66.6	
35–50%	31.0	37.8	35.5	26.6	
<35%	8.9	34.1	9.9	6.8	

LBBB – left bundle branch block; RBBB – right bundle branch block; PCI – percutaneous coronary intervention; CABG – coronary artery bypass grafting; TIA – transient ischemic attack; PAD – peripheral artery disease; COPD – chronic obstructive pulmonary disease; STEMI – ST-elevation myocardial infarction; SBP – systolic blood pressure; LVEF – left ventricular ejection fraction.

Table 2
Treatment, complications and outcome.

	Total n = 3990	LBBB n = 135	RBBB n = 172	Normal QRS n = 3683	p-value
Treatment (%)					
DAPT	91.2	88.9	90.7	91.3	0.621
ACEI/ARB	87.4	88.1	84.9	87.5	0.588
Beta-blockers	83.7	79.3	84.3	83.8	0.358
Statins	91.7	88.9	90.1	91.9	0.336
PCI	81.0	62.2	76.7	81.9	<0.001
Complications (%)					
Mechanical complications	6.4	6.7	9.9	6.2	0.162
Cardiac arrest	7.4	8.1	13.3	7.0	0.016
Complete AV block	2.6	3.0	1.2	2.6	0.474
Major bleeding	0.4	0	1.2	0.4	0.447
Stroke/TIA	1.0	2.2	1.2	1.0	0.338
Outcome (%)					
In-hospital mortality	5.3	8.1	10.5	5.0	0.002
30-day mortality	5.7	8.1	13.4	5.7	<0.001
One-year mortality	9.3	17.0	19.2	8.6	<0.001

DAPT – double antiplatelet treatment; ACEI – angiotensin converting enzyme inhibitor; ARB – angiotensin receptor blocker; PCI – percutaneous coronary intervention; TIA transient ischemic attack.

Table 3
Cox proportional hazard regression analysis (unadjusted and adjusted).

	Univariate	p-value	Multivariate	p-value
Normal QRS	Ref.	–	Ref.	–
LBBB	2.06 (1.35–3.15)	0.001	1.13 (0.72–1.79)	0.584
RBBB	2.37 (1.66–3.4)	<0.001	1.66 (1.14–2.40)	0.007

Results are presented as Hazard ratios and 95% confidence intervals.
Adjusted for: age, heart rate, systolic blood pressure, previous revascularization, diabetes, Killip class ≥2, doubles antiplatelet treatment, renin-angiotensin-aldosterone system blocker, beta-blockers, statins, and percutaneous coronary intervention.

previous myocardial revascularization, heart rate, systolic blood pressure, Killip class and the use of double antiplatelet treatment, renin-angiotensin-aldosterone system antagonists, beta-blockers and statins and percutaneous coronary interventions. After adjustment, LBBB is no longer an independent predictor of all-cause mortality but RBBB remains an important predictor (HR 1.66, $p = 0.007$) (Fig. 1).

3. Discussion

In our sample of patients with ACS, 7.7% of the patients had any form of BBB, particularly RBBB in 4.3%. In general, patients with BBB had worse baseline characteristics, particularly regarding demographic variables, cardiovascular risk factors, previous cardiac history and presentation, with worst data in LBBB patients. Treatment was, however, similar in all groups with the exception of coronary angioplasty, less frequently performed in LBBB, followed by RBBB. The outcome was significantly worse in all form of BBB, but patients with RBBB had higher mortality. In multivariate analysis, and after adjustment, RBBB remains an independent predictor of one-year all-cause mortality.

Our prevalence of RBBB and LBBB is slightly lower than previously reported, particularly when compared with older studies (>10 years) [6,7]. In recent years, however, lower rates have been described, around 4–7% for LBBB and 4–10% for RBBB with our results close to these lower limits [8–10]. Our study only included patients admitted in the Cardiology department, which is a tertiary center, with most patients being referred for invasive treatment strategy. This has important implications in our population, with >50% of patients being STEMI and possibly inducing some referral bias for BBB patients that might explain this discrepancy. In a head-to-head comparison, in non-contemporaneous studies, BBB patients were older, with more comorbidities and heart failure, similar to more recent studies and also to our own results [6–12].

Older studies reported worse outcome in patients with BBB. In-hospital mortality was reported of around 20% and similar in both types of BBB, which was higher when compared to STEMI patients [6,8,11]. In studies with a very long-term follow-up, mortality rates in patients with BBB were 90–94%, much higher when compared to patients with ACS and normal QRS (77%) [9]. A large meta-analysis confirmed that RBBB patients had the highest mortality (in-hospital and long-term), but in this analysis there was considerable heterogeneity across included studies [11]. In more recent studies, mortality rates in this subgroup did not improve much, despite substantial improvements in treatment [10–12]. Studies that compared new/old or persistent/transient BBB, consistently showed that new and permanent BBB (particularly RBBB), was associated with the worst outcome [6,7,12]. Thus, patients with new and permanent BBB are a subset of patients at particularly higher risk and they represent a substantial proportion of patients. In a cohort of patients from 1998 to 2008, new BBB represented 32.5% of all BBB (36% for RBBB and 27% for LBBB) [6]. A more recent cohort (2006–2008) showed lower incidence, with 16% of all RBBB and 13% of all RBBB being new [8]. Permanent BBB is believed to represent 35% of all new RBBB and 40% of all new LBBB [6].

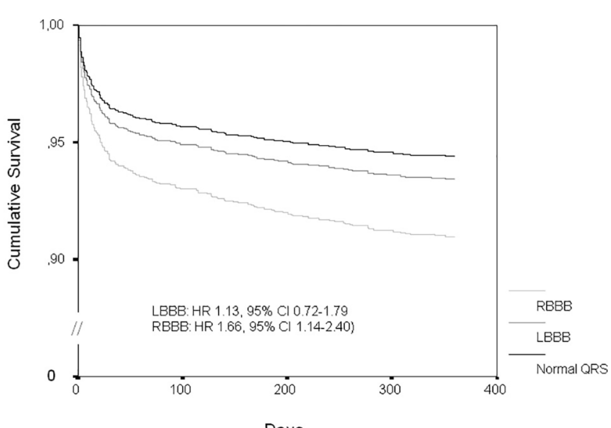
However, those studies have several limitations as already pointed out and a contemporaneous study, with a large real-life population and with head-to-head comparison was necessary to confirm previous information and to validate recent guidelines. Our analysis, in a large cohort of patients, demonstrated that both types of BBB had worse outcome in medium-term follow-up, with in-hospital mortality of 8–10% and one-year all-cause mortality of 17–20%. These results seem to be better that previously reported, probably reflecting the optimized pharmacological treatment with higher use of drugs with important impact in prognosis. However, coronary angioplasty was significantly less performed in BBB patients when compared to normal QRS patients and this is an important cause for the worse results obtained in these groups, particularly in patients with LBBB. In RBBB patients, the outcome was persistently worst, even after adjustment for other independent predictors of mortality. One possible explanation is that these patients had more often cardiac arrest in the index hospitalization. Coronary anatomy might also be an important explanation for the results obtained; in previous studies, angiographic predictors of RBBB were proximal occlusion and TIMI flow 0/1 of the infarct related artery, all known predictors of unfavorable outcome [10]. However, in our study, not all patients were submitted to coronary angiography, particularly in BBB groups, and this information is not available in our data registry. For that reason, it was not possible to assess the impact of coronary anatomy in RBBB incidence and outcome. We believe that there might be some differences in culprit coronary artery or coronary anatomy related to BBB that might have implications in terms of outcome.

3.1. Limitations

This is a retrospective study, with all the limitations previously describe for this type of study. Some information was not possible to collect retrospectively. For instance, it was not possible to assess if BBB was new or old or if it was transient or permanent. We also do not have information about concomitant presence of anterior or posterior left hemiblock with RBBB. Another limitation is the lack of detailed information about quantitative left ventricular ejection fraction, troponins, completeness of revascularization, PCI delays, and concomitant causes of RBBB (such as pulmonary hypertension, pulmonary embolism or right ventricle myocardial infarction). Our sample of patients with BBB is relatively small. The type of follow-up used in the present study did not allowed an analysis of other endpoints, such as myocardial infarction or other cardiovascular events. We only have data for one-year follow-up. A longer follow-up might have provided additional important information.

4. Conclusions

Patients with bundle branch block had worse baseline characteristics, especially patients with left bundle branch block. In long-term



No. at Risk					
Normal QRS	3683	3535	3499	3480	3471
LBBB	135	128	127	126	125
RBBB	172	160	158	157	156

Fig. 1. Multivariate Cox-proportional hazards survival curve.

follow-up, they also had worse outcome, with higher all-cause mortality, particularly in the presence of right bundle branch block. Our results support international recommendations. We should be aware and pay special attention to these patients (particularly with right bundle branch block), and treat them at least as aggressively as patients with normal QRS duration, not only concerning pharmacological treatment but also in terms of invasive strategy.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2018.11.006.

Conflict of interests

None to declare.

References

[1] N. Townsend, L. Wilson, P. Bhatnagar, et al., Cardiovascular diseases in Europe: epidemiological update 2016, Eur. Heart J. 37 (2016) 3232–3245.
[2] A.T. Timoteo, J. Mimoso, On behalf of ProACS investigators. Portuguese registry of acute coronary syndromes (ProACS): 15 years of a continuous and prospective registry, Rev. Port. Cardiol. 37 (2018) 563–573.
[3] G. Steg, S.K. James, D. Atar, et al., ESG guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation, Eur. Heart J. 33 (2012) 2569–2619.
[4] M. Roffi, C. Patrono, J.P. Collet, et al., ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation, Eur. Heart J. 37 (2015) 267–315 2016.
[5] B. Ibanez, S. James, S. Agewall, et al., ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation, Eur. Heart J. 39 (2017) 119–177 2018.
[6] A. Melgarejo-Moreno, J. Galcera-Tomas, L. Consuegra-Sanchez, et al., Relation of new permanent right or left bundle branch block on short- and long-term mortality in acute myocardial infarction bundle branch block and myocardial infarction, Am. J. Cardiol. 116 (2015) 1003–1009.
[7] S. Kurisu, I. Inoue, T. Kawagoe, et al., Right bundle branch block in anterior acute myocardial infarction in the coronary intervention era: acute angiographic findings and prognosis, Int. J. Cardiol. 116 (2007) 57–61.
[8] P. Widimski, F. Rohac, J. Stasek, et al., Primary angioplasty in acute myocardial infarction in right bundle branch block: should new onset right bundle branch block be added to the guidelines as an indicator for reperfusion therapy? Eur. Heart J. 33 (2012) 86–95.
[9] C. Lewinter, C. Torp-Pedersen, J.G.F. Cleland, L. Kober, Right and left bundle branch block as predictors of long-term mortality following myocardial infarction, Eur. J. Heart Fail. 13 (2011) 1349–1354.
[10] J. Li, X. Li, S. Dong, et al., Clinical characteristics and value in early reperfusion therapy for new onset right bundle branch block in patients with acute myocardial infarction, Exp. Ther. Med. 15 (2018) 2620–2626.
[11] L. Xiang, A. Zhang, T. You, J. Chen, W. Xu, M. Shi, Prognostic significance of right bundle branch block in patients with acute myocardial infarction: a systematic review and meta-analysis, Med. Sci. Monit. 22 (2016) 998–1004.
[12] J. Wang, H. Luo, C. Kong, et al., Prognostic value of new-onset right bundle branch block in acute myocardial infarction patients: a systematic review and meta-analysis, Peer J 12 (6) (2018), e4497.
[13] K. Thygesen, J.S. Alpert, A.S. Jaffe, et al., Third universal definition of myocardial infarction, Eur. Heart J. 33 (2012) 2551–2567.